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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/922,958	08/07/2001	Lorenz Poellinger	3743/49008	9818

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EXAMINER

FETTEROLF, BRANDON J

ART UNIT PAPER NUMBER

1642

DATE MAILED: 09/21/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/922,958

Applicant(s)

POELLINGER ET AL.

Examiner

Brandon J. Fetterolf, PhD

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 06 July 2005.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-66 is/are pending in the application.
- 4a) Of the above claim(s) 1-32, 37-39 and 43-66 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 33-36 and 40-42 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____

Response to the Amendment

The Amendment filed on 07/06/2005 in response to the previous Non-Final Office Action (10/29/2004) is acknowledged and has been entered.

Claims 1-66 are currently pending

Claims 1-32, 37-39 and 43-66 are withdrawn from consideration as being drawn to non-elected inventions.

Claims 33-36 and 40-42 are currently under consideration.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office Action.

Formal Matters:

Priority

Upon careful review and reconsideration, the examiner has established a priority date of 08/07/2000 consistent with the provisional application serial number 60/223480 for the instant claims in the application.

Rejections Maintained:

Claims 33-36 and 40-42 **remain** rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement for the reasons set forth in the prior office action (10/29/2004, page 5-7) and for the reasons set forth below.

In reference to the previous action which held that the claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed genus of target proteins, Applicant's assert (Page 10) that the invention relates to methods of screening for agents modulating the function of N-TAD, PYI motif or p564 spanning proteins through analysis of VHL activity, wherein specific examples of molecule in each of these groups as well as the specific activity of interest are described. Applicants further submit that in addition to the material presented in the application, applicants are entitled to rely upon the knowledge and

materials available to the skilled worker when preparing the written description. For example, Applicants contend that while the claimed method is novel over the state of the art, a wealth of information was available to the skilled worker regarding HIF-1 alpha and the Von Hippel-Lindau tumor suppressor protein as of the application filing date, making any additional description in the application superfluous. Along the same lines, Applicants argue that it is known to the skilled workers that the various members of the genus may be evaluated with an agent which is known to be a modulator to ensure that each particular member of the genus will function in the claimed method. Thus, Applicants conclude that the written description, combined with the information available to and knowledge possessed by the skilled worker at the time of application filing sufficiently describes the claimed invention so that it can be practiced in its complete scope without undue experimentation.

These arguments have been considered but are not found persuasive.

First, the Examiner agrees with Applicants assertion that the claims are directed to methods of screening for agents, which modulate the function of N-TAD, PYI motif or p564 spanning proteins through analysis of VHL activity. However, the previous rejection was based on whether the specification described in such a way as to reasonably convey to one skilled in the relevant art that the inventors at the time the application was filed had possession of any and/or all target proteins. Claim 33 recites a method of screening for an agent that modulates the function of a protein comprising an amino acid of SEQ ID NO: 5 comprising incubating a mixture comprising an isolated protein comprising an amino acid of SEQ ID NO: 4 with an altered PYI motif at residues 564-566, a target protein and a candidate agent under conditions whereby, but for the presence of said agent, said isolated protein specifically transactivates reporter genes, or mediates VHL-dependent degradation or physically interact with VHL at a reference affinity (*emphasis added*). Thus, it appears that the isolated protein may interact with a variety of target proteins. For example, Jiang et al. (J. Biol. Chem. 1197; 272: 19253-19260) disclose that Hypoxia-inducible factor 1 (HIF-1) binds to cis-acting hypoxia-response elements within erythropoietin, vascular endothelial growth factor and other genes to activate transcription of hypoxic cells (abstract). However, the written description only reasonably conveys (specification, page 11, paragraph 0035) one species of target proteins, e.g. VHL consisting of SEQ ID NO: 2, to describe the genus of targeting proteins; and therefore is not commensurate with the full scope of any and/or all targeting proteins.

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Lastly, with regards to the Applicants argument pertaining to undue experimentation, Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. §112 is severable from its enablement provision (see page 1115).

In addition to a genus of targeting protein, claim 33, as amended, recites a genus of proteins comprising an amino acid of SEQ ID NO: 5 or 4. In the instant case, all that is required of the protein is that it comprises one amino acid of SEQ ID NO: 5 or 4. However, the instant specification, for reasons of record, fails to provide a written description for any and/or all proteins comprising just one of the amino acid of SEQ ID NO: 5 or 4. (Note: This part of the rejection may be overcome by replacing the term “an” with “the”).

With regards to the rejection applying to currently amended claims 40-42, the claims recite a genus of proteins encoded by at least a fragment of SEQ ID NO: 5 and comprising at least residue 33 of SEQ ID NO: 5. In the instant case, the instant specification fails to describe in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed genus of proteins. Although the claims suggest some functional language, as well as a residue which needs to be retained, the written description only reasonably conveys one protein comprising at least residue 33 of SEQ ID NO: 5, wherein the protein consists of the amino acid sequence of SEQ ID NO: 4 and two fragments thereof (SEQ ID NOs: 5 and 6), and therefore, is not commensurate with the full scope of any and/or all proteins encoded by at least a fragment of SEQ ID NO: 5 and comprising at least residue 33 of SEQ ID NO: 5.

New Objections:

Claim Objections

Claims 33-36 are objected to because of the following informalities: In claim 33, it appears that the word “the” should be inserted between the words modulates and function. Appropriate correction is required.

New Rejections:

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 40-42 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In the instant case, claim 40 is drawn to a method of evaluating an antagonist of the PYI motif or a protein encoded by at least a fragment of SEQ ID NO: 5 and comprising at least residue 33 of SEQ ID NO: 5. However, the sequence represented as SEQ ID NO: 5 is an amino acid sequence and not a nucleic acid sequence which encodes a protein. Thus, it is unclear what applicants are attempting to claim.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 40-42 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. THIS IS A NEW MATTER REJECTION.

In the instant case, claim 40 refers to a method of evaluating an antagonist of the PYI motif or a protein encoded by at least a fragment of SEQ ID NO: 5 and comprising at least residue 33 of SEQ ID NO: 5. However, a careful review of the specification as originally filed does not appear to have support for the specific limitation a protein encoded by at least a fragment of SEQ ID NO: 5 and comprising at least residue 33 of SEQ ID NO: 5. Applicant is invited to point to clear support or specific examples of the claimed limitation in the specification as-filed or remove such

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amendatory language in response to this action.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 40-42 are rejected under 35 U.S.C. 102(b) as being anticipated by Maxwell et al. (Nature 1999; 399: 271-275, IDS).

Maxwell discloses a method of evaluating an antagonist of the PYI motif for VHL-HIF-1 alpha interacting inhibiting efficacy; comprising: determining a reference level of VHL-HIF-1 alpha interacting in a cell or group of cells; administering said antagonist to an equivalent test cell; measuring the level of VHL-HIF-1 alpha interaction in said test cell; and determining said antagonist is efficacious when the measured test level of VHL-HIF-1 alpha interaction is less than the reference level of VHL-HIF-1 alpha interaction (page 273, 1st column, 1st full paragraph to 2nd column). The reference further teaches that the test were done at both normoxic and hypoxic conditions (page 273, 1st column, 1st full paragraph to 2nd column). Thus, while the Maxwell et al. does not specifically state that the inhibitor is an agonist of the PYI motif, the claimed functional limitation would be an inherent property of the referenced method because as evidenced by Tanimoto et al. (EMBO 2000; 19: 4298-4309, IDS), the highly conserved core motif, i.e. PYI, of the N-TAD of HIF-1 alpha is critical for interaction with VHL (specifically page 4303, 1st column, 1st full paragraph). Thus, it does not appear that the claim language or limitation results in a manipulative difference in the method steps when compared to the prior art disclosure. See Bristol-Myers Squibb Company v. Ben Venue Laboratories 58 USPQ2d 1508 (CAFC 2001).

Therefore, NO claim is allowed

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All other rejections and/or objections are withdrawn in view of applicant's amendments and arguments there to.


Any inquiry concerning this communication or earlier communications from the examiner should be directed to Brandon J. Fetterolf, PhD whose telephone number is (571)-272-2919. The examiner can normally be reached on Monday through Friday from 8:30 to 5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeff Siew can be reached on 571-272-0787. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Brandon J Fetterolf, PhD
Examiner
Art Unit 1642

BF


JEFFREY SIEW
SUPERVISORY PATENT EXAMINER
9/16/05